

A simplified method of giving rabies vaccine

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A simplified economical method of giving rabies vaccine is just as effective as the expensive standard vaccine regimen at stimulating anti-rabies antibodies.

A clinical trial in healthy volunteers has found that a simpler and cheaper way of using rabies vaccines proved to be just as effective as the current most widely used method at stimulating antibodies against rabies. The trial is published in this week's *PLoS Neglected Tropical Diseases*.

Dr Mary Warrell (Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, United Kingdom) and colleagues, who conducted the trial with a vaccine in routine use, say that the simplified method has the advantages of requiring fewer clinic visits, being more practicable, and acceptable, and having a wider margin of safety, especially in inexperienced hands. It would therefore, they say, be "suitable for use anywhere in the world where there are financial constraints, and especially where two or more patients are likely to be treated on the same day."

All human deaths from rabies result from failure to give adequate prophylaxis. After a rabid animal bite, immediate wound cleaning, rabies vaccine and injections of anti-rabies antibody (immunoglobulin) effectively prevent fatal infection. But anti-rabies immunoglobulin is very rarely available in developing countries, and so prevention relies on giving people bitten by rabid animals effective vaccine treatment.

The vaccines that are currently approved by the World Health

Organization, which are usually injected into the muscle, are prohibitively expensive, and so are unaffordable in developing countries. In Africa, for example, the average cost of an intramuscular course of vaccine is \$US 39.6, equivalent to 50 days' wages.

Two economical regimens, involving injecting small amounts of vaccine into the skin (intradermally) at 2 or 8 sites on the first day of the course, with subsequent booster doses are available in a few places. With the 8-site method, a large dose of vaccine is given on the first day only, whereas with the 2-site method the same dose is divided between the first and third days, entailing an extra visit to the clinic. However, practical or perceived difficulties have restricted widespread uptake of these economical methods. Dr Warrell and colleagues therefore set out to test a new, similar simplified regimen, involving injections at 4 sites on the first day.

They vaccinated healthy volunteers to compare the antibody levels induced by the 4-site intradermal regimen with those induced by the current 2-site and 8-site intradermal regimens and the "gold standard" intramuscular regimen favored internationally. All of the economical intradermal regimens worked just as well as the intramuscular method at stimulating anti-rabies antibodies.

The authors conclude that the results provide sufficient evidence that the simplified 4-site regimen now meets all the criteria necessary for its recommendation for use wherever the cost of vaccine is prohibitive.

Citation: Warrell MJ, Riddell A, Yu L-M, Phipps J, Diggle L, et al. (2008) A Simplified 4-Site Economical Intradermal Post-Exposure Rabies Vaccine Regimen: A Randomised Controlled Comparison with Standard Methods. PLoS Negl Trop Dis 2(4): e224. doi:10.1371/journal.pntd.0000224

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